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**Applicant's Name:** John P. McKearn et al.

**Reissue Serial No.:** 09/857,873 **Examiner:** Rebecca Cook

**Filing Date:** October 5, 2001 **Art Unit:** 1614

**Application Title:** METHOD OF USING A CYCLOOXYGENASE-2 INHIBITOR AND ONE OR MORE ANTINEOPLASTIC AGENTS AS A COMBINATION THERAPY IN THE TREATMENT OF NEOPLASIA

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0IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Application of J.P. McKearn et al. Art Unit 1614
Serial No. 09/857,873
Filed October 5, 2001
Confirmation No. 2817
For METHOD OF USING A CYCLOOXYGENASE-2 INHIBITOR AND ONE OR MORE ANTINEOPLASTIC AGENTS AS A COMBINATION THERAPY IN THE TREATMENT OF NEOPLASIA
Examiner Rebecca Cook

January 21, 2004

**SUPPLEMENT TO AMENDMENT B AND RESPONSE TO OFFICE ACTION**

TO THE COMMISSIONER FOR PATENTS,

SIR:

This response is being filed in response to the Office action mailed August 7, 2003, and to supplement the Amendment B and Response to Office action filed November 7, 2003.

## I. 35 U.S.C. 103(a) Rejection

In addition to Applicants' argument that there is no motivation to combine the prior art cited by the Office (as detailed in Amendment B), Applicants are submitting with this response two journal articles, Crane et al.[1], and Smith et al.[2], that each disclose unexpected results for the claimed combination of celecoxib and gemcitabine.

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[1]Crane et al., (2003) Am J Clin Oncol 26(4 suppl 2):S:81-S84.

[2]Smith et al., "Preliminary report of a phase II trial of gemcitabine combined with celecoxib for advanced pancreatic cancer" (Proc Am Soc Clin Oncol (2003) 22: page 374, Abstract No: 1502).

Briefly, Crane et al. test a number of different treatment regimes in a murine sarcoma model for pancreatic cancer.[3] In particular, Figure 1 on page S82 discloses the impact on tumor size after administration of celecoxib alone, vehicle alone, gemcitabine alone, radiation alone (i.e, 30 Gy), celecoxib in combination with gemcitabine, celecoxib in combination with radiation, gemcitabine in combination with radiation, and celecoxib in combination with radiation and gemcitabine. In view of their results, Crane et al. report that "celecoxib and gemcitabine on their own caused tumor growth delay for several days, ***but when combined their effect was additive.***"[4]

In addition, it is reported in Smith et al. that "a combination of gemcitabine and celecoxib is active and well tolerated in patients with advanced pancreatic cancer."

The disclosure of Crane et al. and Smith et al. demonstrates the beneficial combination of celecoxib and gemcitabine, as compared to either compound administered alone, for use in treating or preventing neoplasia. Evidence of superior results not disclosed in the prior art is sufficient to establish non-obviousness.[5] In view of the superior results demonstrated by the applicants for the claimed combination, claim 1 is patentable over the cited art.

## II. Conclusion

In light of the foregoing, Applicants request entry of the attached publications along with the supplemental information disclosure enclosed with this response. Applicants also solicit an allowance of the claims. The Examiner is invited to contact the undersigned attorney should any issues remain unresolved.

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[3]Crane et al., (2003) Am J Clin Oncol 26(4 suppl 2):S:81-S84.

[4]Crane et al., at page S82, column 2 (emphasis added); and Figure 1.

[5]See In re Chupp, 816 F.2d 643, 646, 2 USPQ2d 1437 (Fed. Cir. 1987) and cases cited therein.

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The Commissioner is hereby authorized to charge any fees associated with this Response to Deposit Account 19-1345.

Respectfully submitted,

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